10/767,645 EAST

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	2243	((514/267) or (514/259.3) or (514/293) or (514/303) or (514/393)). CCLS.	US-PGPUB; USPAT	OR	OFF	2005/12/02 11:22
L2	959	((544/281) or (548/303.1) or (548/250) or (548/258) or (548/262. 4)).CCLS.	US-PGPUB; USPAT	OR	OFF	2005/12/02 11:24
L3	1469	((546/82) or (546/84) or (546/118)). CCLS.	US-PGPUB; USPAT	OR	OFF	2005/12/02 11:25
L4	3798	L1 or L2 or L3	US-PGPUB; USPAT	OR	OFF	2005/12/02 11:25
L5	823	L4 and imidazo	US-PGPUB; USPAT	OR	OFF	2005/12/02 11:25
L6	774	L5 and (phenyl or pyridyl or pyridinyl)	US-PGPUB; USPAT	OR	OFF	2005/12/02 11:26

10/ 767,645

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1202txn

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	SEP 09	ACD predicted properties enhanced in REGISTRY/ZREGISTRY
NEWS 4	OCT 03	MATHDI removed from STN
NEWS 5	OCT 04	CA/CAplus-Canadian Intellectual Property Office (CIPO) added to core patent offices
NEWS 6	OCT 13	New CAS Information Use Policies Effective October 17, 2005
NEWS 7	OCT 17	STN(R) AnaVist(TM), Version 1.01, allows the export/download of CAplus documents for use in third-party analysis and visualization tools
NEWS 8	OCT 27	Free KWIC format extended in full-text databases
NEWS 9	OCT 27	DIOGENES content streamlined
NEWS 10	OCT 27	EPFULL enhanced with additional content
NEWS 11	NOV 14	CA/CAplus - Expanded coverage of German academic research
NEWS 12	NOV 30	REGISTRY/ZREGISTRY on STN(R) enhanced with experimental spectral property data

NEWS EXPRESS NOVEMBER 18 CURRENT VERSION FOR WINDOWS IS V8.01,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005.
V8.0 USERS CAN OBTAIN THE UPGRADE TO V8.01 AT
http://download.cas.org/express/v8.0-Discover/

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:07:35 ON 02 DEC 2005

=> file reg
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION

10/ 767,645

FULL ESTIMATED COST 0.21 0.21

FILE 'REGISTRY' ENTERED AT 11:07:56 ON 02 DEC 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 30 NOV 2005 HIGHEST RN 869059-01-8
DICTIONARY FILE UPDATES: 30 NOV 2005 HIGHEST RN 869059-01-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

```
**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from  *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
**********************************************************************
```

Structure search iteration limits have been increased. See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.43	0.64

FILE 'REGISTRY' ENTERED AT 11:08:04 ON 02 DEC 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 30 NOV 2005 HIGHEST RN 869059-01-8
DICTIONARY FILE UPDATES: 30 NOV 2005 HIGHEST RN 869059-01-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

```
**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10767645.str
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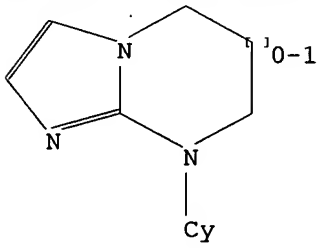
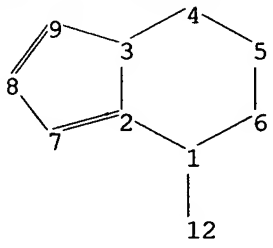




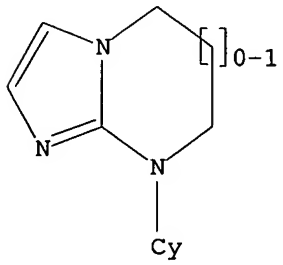

```
chain nodes :
12
ring nodes :
1  2  3  4  5  6  7  8  9
chain bonds :
1-12
ring bonds :
1-2  1-6  2-3  2-7  3-4  3-9  4-5  5-6  7-8  8-9
exact/norm bonds :
1-2  1-6  1-12  2-3  2-7  3-4  3-9  4-5  5-6  7-8
exact bonds :
8-9
isolated ring systems :
containing 1 :


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  12:Atom
Generic attributes :
12:
Saturation             : Unsaturated
Number of Carbon Atoms : less than 7
Type of Ring System    : Monocyclic

Element Count :
Node 12: Limited
    C,C5-6
    N,N0-1
```

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 sample
SAMPLE SEARCH INITIATED 11:08:46 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 780 TO ITERATE

100.0% PROCESSED 780 ITERATIONS 29 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 13925 TO 17275
PROJECTED ANSWERS: 257 TO 903

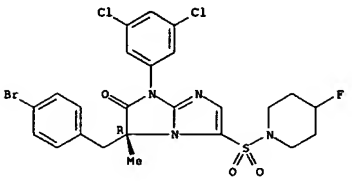
L2 29 SEA SSS SAM L1

=> d scan l2

10/ 767,645

L2 29 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
IN Piperidine, 1-[[(3R)-3-[(4-bromophenyl)methyl]-1-(3,5-dichlorophenyl)-2,3-dihydro-3-methyl-2-oxo-1H-imidazo[1,2-a]imidazol-5-yl]sulfonyl]-4-fluoro-(9CI)
MF C24 H22 Br Cl2 F N4 O3 S

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

10/ 767,645

=> s l1 full
FULL SEARCH INITIATED 11:09:02 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 16730 TO ITERATE

100.0% PROCESSED 16730 ITERATIONS 651 ANSWERS
SEARCH TIME: 00.00.01

L3 651 SEA SSS FUL L1

=> file hcaplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 161.76 162.40

FILE 'HCAPLUS' ENTERED AT 11:09:13 ON 02 DEC 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 2 Dec 2005 VOL 143 ISS 24
FILE LAST UPDATED: 1 Dec 2005 (20051201/ED)

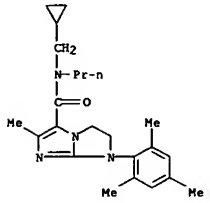
New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 16 L3

=> d l4 1- ibib abs fhitstr
YOU HAVE REQUESTED DATA FROM 16 ANSWERS - CONTINUE? Y/(N):y

L4 ANSWER 1 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:708476 HCAPLUS
DOCUMENT NUMBER: 143:347100
TITLE: Synthesis, structure-activity relationships, and anxiolytic activity of 7-aryl-6,7-dihydroimidazoimidazole corticotropin-releasing factor 1 receptor antagonists
AUTHOR(S): Han, Xiaojun; Michne, Jodi A.; Pin, Sokhom S.; Burris, Kevin D.; Balanda, Lynn A.; Fung, Lawrence K.; Fiedler, Tracey; Browman, Kaitlin E.; Taber, Matthew T.; Zhang, Jie; Dubowchik, Gene M.
CORPORATE SOURCE: Pharmaceutical Research Institute, Bristol-Myers Squibb Company, Wallingford, CT, 06492, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(17), 3870-3873
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 7-Aryl-6,7-dihydro imidazoimidazole derivs. represent a novel series of high-affinity corticotropin-releasing factor 1 receptor antagonists. Here, their synthesis and structure-activity relationship as well as the behavioral activity of two exemplary compds. in a mouse canopy model of anxiety are reported.
IT **444321-95-3P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (aryl)dihydro imidazoimidazole derivs. and study of their structure-activity relationship, their anxiolytic activity, and activity as corticotropin-releasing factor 1 receptor antagonists)
RN 444321-95-3 HCAPLUS
CN 1H-Imidazo[1,2-a]imidazole-5-carboxamide, N-(cyclopropylmethyl)-2,3-dihydro-6-methyl-N-propyl-1-(2,4,6-trimethylphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

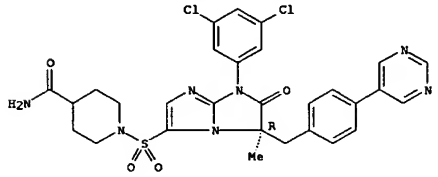
L4 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:177881 HCAPLUS
DOCUMENT NUMBER: 142:274025
TITLE: Methods using a combination of a p38 MAP kinase inhibitor with another active agent for the treatment of chronic obstructive pulmonary disease (COPD) and pulmonary hypertension
INVENTOR(S): Gupta, Abhya; Iacono, Philippe Didier; Kelash-Cannavo, Linda Jean; Madwed, Jeffrey B.; Park, Jung-Yong; Way, Susan Lynn; Yazdanian, Mehran
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA; Boehringer Ingelheim Pharma GmbH & Co. KG; Boehringer Ingelheim France S.A.S.
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005018624	A2	20050303	WO 2004-US27013	20040819
WO 2005018624	A3	20050506		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005148555	A1	20050707	US 2004-921448	20040819

PRIORITY APPLN. INFO.: US 2003-497376P P 20030822
AB Methods are disclosed for treating COPD and pulmonary hypertension using p38 MAP Kinase inhibitors in combination with one or more other active ingredients.
IT **321656-57-9**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(p38 MAP kinase inhibitor combination with another active agent for treatment of chronic obstructive pulmonary disease and pulmonary hypertension)
RN 321656-57-9 HCAPLUS
CN 4-Piperidinecarboxamide, 1-[[(3R)-1-(3,5-dichlorophenyl)-2,3-dihydro-3-methyl-2-oxo-3-[[4-(5-pyrimidinyl)phenyl]methyl]-1H-imidazo[1,2-a]imidazol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

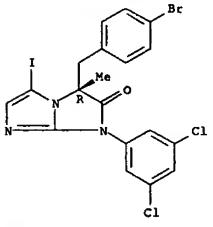
Absolute stereochemistry.

L4 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L4 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:168805 HCAPLUS
DOCUMENT NUMBER: 142:410694
TITLE: Alkylation of Magnesium Sulfinates: A Direct Transformation of Functionalized Aromatic/Heteroaromatic Halides into Sulfones
AUTHOR(S): Wu, Jiang-Ping; Emeigh, Jonathan; Su, Xi-Ping
CORPORATE SOURCE: Department of Medicinal Chemistry, Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT, 06877, USA
SOURCE: Organic Letters (2005), 7(7), 1223-1225
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:410694
AB Sulfinate alkylation is one of the conventional methods for sulfone synthesis. The alkylation of magnesium sulfinates, which are easily accessible via reactions of organomagnesium intermediates with sulfur dioxide, provides a convenient route for sulfone preparation In this communication, the authors report a preliminary study of the alkylation of arylmagnesium sulfinates. An application of this reaction to directly transform functionalized aromatic/heteroarom. halides into sulfones is also described.
IT **321656-73-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of sulfones via generation of Grignard reagents from aromatic/heteroarom. halides by magnesium-halide exchange followed by reaction with sulfur dioxide and alkylation of the magnesium sulfinate intermediates)
RN 321656-73-9 HCAPLUS
CN 1H-Imidazo[1,2-a]imidazol-2(3H)-one, 3-[(4-bromophenyl)methyl]-1-(3,5-dichlorophenyl)-5-iodo-3-methyl-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

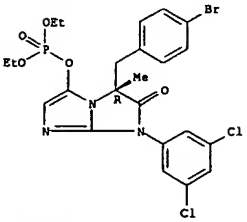


REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:41390 HCAPLUS
DOCUMENT NUMBER: 142:299796
TITLE: Development of a Scalable Process for 1-(3,5-Dichlorophenyl)-5-iodo-3-methyl-(4-methylbenzyl)-1H-imidazo[1,2-a]imidazol-2-one: A Key Intermediate for the Synthesis of LFA-1 Inhibitors
AUTHOR(S): Frutos, Rogelio P.; Eriksson, Magnus; Wang, Xiao-Jun; Byrne, Denis; Varsolona, Richard; Johnson, Michael D.; Nummy, Lawrence; Krishnamurthy, Dhileepkumar; Senanayake, Chris H.
CORPORATE SOURCE: Department of Chemical Development, Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, 06877-0368, USA
SOURCE: Organic Process Research & Development (2005), 9(2), 137-140
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A safe, robust, chromatog.-free and reproducible process for the multi-kilogram synthesis of 3-(4-bromobenzyl)-1-(3,5-dichlorophenyl)-5-iodo-3- methyl-1H-imidazo[1,2-a]imidazol-2-one, a key intermediate for the synthesis of LFA-1 inhibitors, was developed and implemented at pilot plant scale. The process allowed support of preclin. activities in the LFA-1 program. Major improvements were realized by lowering the reaction temperature to -15° and changing the solvent from dichloromethane to acetonitrile, and using TMSI/NaI as reagent system for regioselective hydroiodination. Under the improved conditions, the HI catalyzed proto-deiodination pathway of the intermediate was minimized and the intermediate was obtained in high yield and with low impurity profile.
IT **397329-89-4P**
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; pilot-scale process for preparation of dichlorophenyliodomethylbenzylimidazoimidazolone key intermediate for synthesis of LFA-1 inhibitors)
RN 397329-89-4 HCAPLUS
CN Phosphoric acid, (3R)-3-[(4-bromophenyl)methyl]-1-(3,5-dichlorophenyl)-2,3-dihydro-3-methyl-2-oxo-1H-imidazo[1,2-a]imidazol-5-yl diethyl ester (9CI) (CA INDEX NAME)

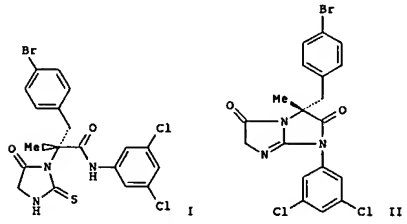
Absolute stereochemistry.

L4 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1068436 HCAPLUS
DOCUMENT NUMBER: 142:197972
TITLE: A practical synthesis of LFA-1 inhibitors utilizing CuCl-promoted intramolecular cyclization of thiohydantoins
AUTHOR(S): Wang, Xiao-jun; Zhang, Li; Xu, Yibo; Krishnamurthy, Dhileepkumar; Varsolona, Richard; Nummy, Laurence; Shen, Sherry; Frutos, Rogelio P.; Byrne, Denis; Chung, J. C.; Farina, Vittorio; Senanayake, Chris H.
CORPORATE SOURCE: Chemical Development Department, Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, 06877-0368, USA
SOURCE: Tetrahedron Letters (2005), 46(2), 273-276
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:197972
GI



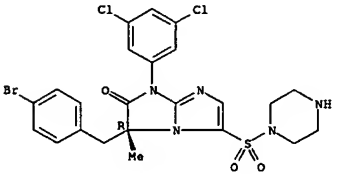
I

II

AB An efficient and chromatog.-free approach for synthesis of a new class of LFA-1 (antigen) inhibitors was developed. These compds. are potential inflammation inhibitors (no data). A copper(I) chloride-promoted intramol. cyclization of thiohydantoins serves as a key step to highly functionalized bicyclic guanidines, that were subsequently converted to 1H-imidazo[1,2-a]imidazol-2-one LFA-1 inhibitors. This process has been successfully implemented in the pilot plant to produce multi-kilogram quantities of 1H-imidazo[1,2-a]imidazol-2-one LFA-1 inhibitors. The copper chloride (CuCl)-mediated cyclization of a thiourea derivative (I) gave (3R)-3-[(4-bromophenyl)methyl]-1-(3,5-dichlorophenyl)-3-methyl-1H-imidazo[1,2-a]imidazole-2,5(3H,6H)-dione (II) in 85-92% yield.
IT **321656-61-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of {{(R)-[(bromophenyl)methyl][di(chloro)phenyl]dihydro(methyl)(oxo)imidazo[1,2-a]imidazolyl]sulfonyl]piperazine (bicyclic guanidine) using copper chloride-promoted cyclization of thiourea derivative as key synthetic step)
RN 321656-61-5 HCAPLUS

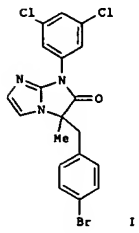
L4 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
CN Piperazine, 1-[[(3R)-3-[(4-bromophenyl)methyl]-1-(3,5-dichlorophenyl)-2,3-dihydro-3-methyl-2-oxo-1H-imidazo[1,2-a]imidazol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:790832 HCAPLUS
DOCUMENT NUMBER: 142:6469
TITLE: Second-generation lymphocyte function-associated antigen-1 inhibitors: 1H-imidazo[1,2-α]imidazol-2-one derivatives
AUTHOR(S): Emeigh, Jonathan; Gao, Donghong A.; Goldberg, Daniel R.; Kuzmich, Daniel; Miao, Clara; Potocki, Ian; Qian, Kevin C.; Sorcek, Ronald J.; Jeanfavre, Deborah D.; Kishimoto, Kei; Mainolfi, Elizabeth A.; Nabozny, Gerald, Jr.; Reilly, Patricia; Rothlein, Robert; Sellati, Rosemarie H.; Woska, Joseph R., Jr.; Chen, Shirlynn; Gunn, Jocelyn A.; O'Brien, Drane; Norris, Stephen H.; Kelly, Terence A.; Peng, Charline; Wu, Jiang-Ping
CORPORATE SOURCE: Research and Development, Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT, 06877, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(22), 5356-5366
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:6469
GI

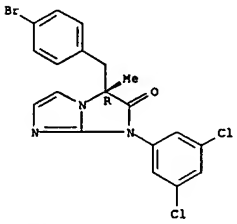


I

AB A novel class of lymphocyte function-associated antigen-1 (LFA-1) inhibitors is described. Discovered during the process to improve the physicochem. and metabolic properties of BIRT377, a previously reported hydantoin-based LFA-1 inhibitor, these compds. are 5- or 6-substituted derivs. of the 1H-imidazo[1,2-α]imidazol-2-one I. The structure-activity relationship (SAR) shows that electron-withdrawing groups at C(5) on the imidazole ring benefit potency and that oxygen-containing functional groups attached to a C(5)-sulfonyl or sulfonamide group further improve potency. This latter gain in potency is attributed to the interaction(s) of the

L4 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
functionalized sulfonyl/sulfonamide groups with the protein, likely polar-polar in nature, as suggested by SAR data. X-ray studies revealed that these bicyclic inhibitors bind to the I-domain of LFA-1 in a pattern similar to that of BIRT377.
IT 321656-72-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1H-imidazo[1,2-α]imidazol-2-ones as second-generation lymphocyte function-associated antigen-1 inhibitors)
RN 321656-72-8 HCAPLUS
CN 1H-Imidazo[1,2-a]imidazol-2(3H)-one, 3-[(4-bromophenyl)methyl]-1-(3,5-dichlorophenyl)-3-methyl-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

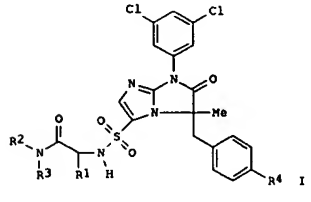


REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:412950 HCAPLUS
DOCUMENT NUMBER: 140:423947
TITLE: Preparation of [6,7-dihydro-5H-imidazo[1,2-a]imidazole-3-sulfonylamino]propionamide derivatives for treatment of inflammatory disease
INVENTOR(S): Kelly, Terence Alfred; Kim, Jin Mi; Lemieux, Rene Marc
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004041827	A2	20040521	WO 2003-US33865	20031027
WO 2004041827	A3	20040715		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004127534	A1	20040701	US 2003-686073	20031015
US 6844360	B2	20050118		
CA 2504219	AA	20040521	CA 2003-2504219	20031027
EP 1560830	A2	20050810	EP 2003-779257	20031027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003015836	A	20050913	BR 2003-15836	20031027
US 2005054703	A1	20050310	US 2004-969105	20041020
US 2005165027	A1	20050728	US 2005-34701	20050113
PRIORITY APPLN. INFO.:			US 2002-422446P	P 20021030
			US 2003-686073	A3 20031015
			WO 2003-US33865	W 20031027

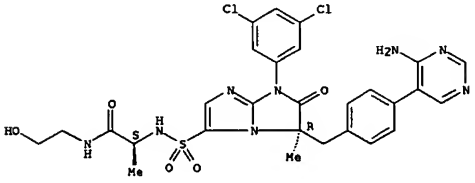
OTHER SOURCE(S): MARPAT 140:423947
GI



I

L4 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
AB The invention relates to imidazo[1,2-a]imidazole amino acid derivs. I [R1 is alkyl optionally mono- or disubstituted by oxo or morpholino; R2, R3 are H or alkyl mono- or disubstituted by CONH2 or OH or R2R3N is piperazinyl; R4 is cyano, trifluoromethoxy, pyrimidinyl or mono- or diaminopyrimidinyl] or their pharmaceutically-acceptable salts which exhibit good inhibitory effect upon the interaction of cellular adhesion mols. (CAMs) and leukointegrins and are thus useful in the treatment of inflammatory disease. Thus, I [R2R3NCOCHR1NH is L-alaninamide residue (R ring stereo)] was prepared from (R)-3-(4-bromobenzyl)-1-(3,5-dichlorophenyl)-3-methyl-1H-imidazo[1,2-a]imidazol-2-one by cyanation with Zn(CN)2, conversion to the sulfonyl chloride (iodination with N-iodosuccinimide, reaction with cyclopentylmagnesium chloride, SO2 and N-chlorosuccinimide), and condensation with L-alaninamide hydrochloride. Synthesized I showed Kd < 10 μM for inhibition of integrin LFA-1 and ICAM-1.
IT 688755-94-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of [(dihydroimidazoimidazolesulfonyl)amino]propionamide derivs. for treatment of inflammatory disease)
RN 688755-94-4 HCAPLUS
CN Propanamide, 2-[[[(3R)-3-[[4-(4-amino-5-pyrimidinyl)phenyl]methyl]-1-(3,5-dichlorophenyl)-2,3-dihydro-3-methyl-2-oxo-1H-imidazo[1,2-a]imidazol-5-yl]sulfonyl]amino]-N-(2-hydroxyethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



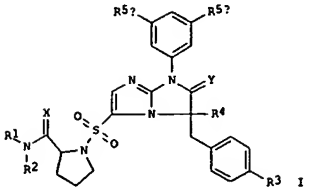
L4 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:412808 HCAPLUS
DOCUMENT NUMBER: 140:423673
TITLE: Preparation of derivatives of [6,7-dihydro-5H-imidazo[1,2-a]imidazole-3-sulfonyl]-pyrrolidine-2-carboxylic acid amide as anti-inflammatory agents
INVENTOR(S): Kelly, Terence Alfred; Kim, Jin Mi; Lemieux, Rene Marc; Tschantz, Matt Aaron
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004041273	A1	20040521	WO 2003-US33966	20031027
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 6852748	B1	20050208	US 2003-685638	20031015
CA 2504131	AA	20040521	CA 2003-2504131	20031027
EP 1558248	A1	20050803	EP 2003-777910	20031027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005054704	A1	20050310	US 2004-969698	20041020

PRIORITY APPLN. INFO.:
US 2002-422449P P 20021030
US 2003-685638 A3 20031015
WO 2003-US33966 W 20031027

OTHER SOURCE(S): MARPAT 140:423673
GI

L4 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



I

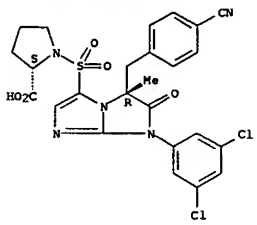
AB The title compds. [I; R1, R2 = hydrogen (provided that R1 and R2 are not both hydrogen atoms), each (un)substituted straight or branched C1-7 alkyl, C3-6 cycloalkyl, aryl (selected form the group consisting of biphenyl, Ph, or quinolinyl), or unsatd. or partially saturated heterocyclic group containing 2 to 3 C, 1 to 2 N, 0 to 1 S, and 0 to 1 O atoms; or wherein R1 and R2 constitute a saturated 3 to 5-methylene group bridge which together with the nitrogen atom between them form (un)substituted heterocyclic ring; R3 = (un)substituted aryl (selected from the group consisting of pyridyl and pyrimidyl), CF3O, cyano; R4 = straight or branched C1-3 alkyl; R5a, R5b = Cl, CF3; X, Y = O, S; Y] or pharmaceutically acceptable salts thereof are prepared These compds. exhibit good inhibitory effect upon the interaction of cellular adhesion mols. (CAMs) and leukointegrins and are thus useful in the treatment of inflammatory disease including adult respiratory distress syndrome, shock, oxygen toxicity, multiple organ injury syndrome secondary to septicemia, multiple organ injury syndrome secondary to trauma, reperfusion injury of tissue due to cardiopulmonary bypass, myocardial infarction [associated with use of thrombolysis agents (sic)], acute glomerulonephritis, vasculitis, reactive arthritis, dermatosis with acute inflammatory components, stroke, thermal injury, hemodialysis, leukapheresis, ulcerative colitis, necrotizing enterocolitis, granulocyte transfusion associated syndrome, psoriasis, organ/tissue transplant rejection, graft vs. host reactions, autoimmune diseases (including Raynaud's syndrome, autoimmune thyroiditis, dermatitis, multiple sclerosis, rheumatoid arthritis, insulin-dependent diabetes mellitus, uveitis, inflammatory bowel disease, Crohn's disease, ulcerative colitis or systemic lupus erythematosus), asthma, or the toxic effects of cytokine therapy. Thus, a solution of (R)-3-(3,5-dichlorophenyl)-5-methyl-2-thioxo-5-(4-trifluoromethoxybenzyl)imidazolidin-4-one and aminoacetaldehyde dimethylacetal (6.50 mL, 59.7 mmol) in MeOH was treated with aqueous tert-Bu hydroperoxide solution over 25 min at <20° under ice-cooling, kept at the same temperature for 1 h , warmed to room temperature, and stirred for 86 h to give (R)-3-(3,5-dichlorophenyl)-2-[[(E)-2,2-dimethoxyethyl)imino]-5-methyl-5-(4-trifluoromethoxybenzyl)imidazolidin-4-one which was heated in the presence of p-MeC6H4SO3H in acetone at reflux for 2 h to give (R)-1-(3,5-dichlorophenyl)-3-methyl-3-(4-trifluoromethoxybenzyl)-1H-imidazo[1,2-a]imidazol-2-one.

L4 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

IT 321656-41-1P, (S)-1-[[(R)-5-(4-Cyanobenzyl)-7-(3,5-dichlorophenyl)-5-methyl-6-oxo-6,7-dihydro-5H-imidazo[1,2-a]imidazol-3-yl]sulfonyl]pyrrolidine-2-carboxylic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of [dihydro-5H-imidazo[1,2-a]imidazolylsulfonyl]pyrrolidinecarboxylic acid amide derivs. for treatment of inflammatory diseases)

RN 321656-41-1 HCAPLUS
CN L-Proline, 1-[[(3R)-3-[(4-cyanophenyl)methyl]-1-(3,5-dichlorophenyl)-2,3-dihydro-3-methyl-2-oxo-1H-imidazo[1,2-a]imidazol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:142968 HCAPLUS
DOCUMENT NUMBER: 140:193056
TITLE: Combinations of active agents with p38 MAP kinase inhibitors, pharmaceutical compositions, and use in the treatment of cytokine-mediated diseases
INVENTOR(S): Simianer, Stefan; Bilbault, Pascal; Cappola, Michael L.; Way, Susan Lynn
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA; Boehringer Ingelheim France
SOURCE: PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014387	A1	20040219	WO 2003-US25341	20030812
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004110755	A1	20040610	US 2003-638702	20030811
CA 2497448	AA	20040219	CA 2003-2497448	20030812
EP 1530477	A1	20050518	EP 2003-785255	20030812
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.:
US 2002-403115P P 20020813
WO 2003-US25341 W 20030812

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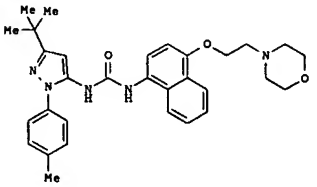
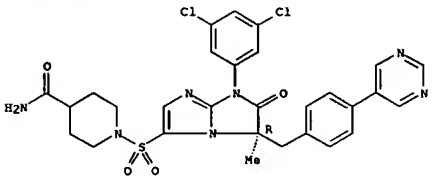


I

AB The invention relates to pharmaceutical combination therapies based on p38 kinase inhibitors and another active ingredients, pharmaceutical compns. comprising such combinations, processes for preparing them, and their use in the treatment of cytokine-mediated diseases. Preparation of I (BIRB 796 BS) is

L4 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
described.
IT 321656-57-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations of active agents with p38 MAP kinase inhibitors, pharmaceutical compns., and use in treatment of cytokine-mediated diseases)
RN 321656-57-9 HCAPLUS
CN 4-Piperidinecarboxamide, 1-[[(3R)-1-(3,5-dichlorophenyl)-2,3-dihydro-3-methyl-2-oxo-3-[[4-(5-pyrimidinyl)phenyl]methyl]-1H-imidazo[1,2-a]imidazol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



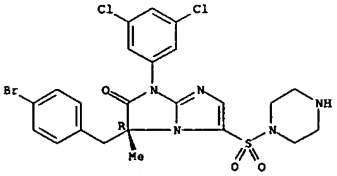
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:597593 HCAPLUS
DOCUMENT NUMBER: 139:276851
TITLE: Regiocontrolled synthesis of highly-functionalized fused imidazoles: a novel synthesis of second generation LFA-1 inhibitors
AUTHOR(S): Frutos, Rogelio P.; Johnson, Michael
CORPORATE SOURCE: Department of Chemical Development, Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, 06877-0368, USA
SOURCE: Tetrahedron Letters (2003), 44(34), 6509-6511
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:276851
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A new and reliable route to a new class of LFA-1 inhibitors such as I has been developed. A key aspect of this route is the transformation of amino amide II into iodide III in four steps. Iodide III is a key advanced intermediate used in the synthesis of all second-generation 1H-imidazo[1,2-a]imidazol-2-one LFA-1 inhibitors.
IT 321656-61-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(regiocontrolled synthesis of fused imidazoles)
RN 321656-61-5 HCAPLUS
CN Piperazine, 1-[[(3R)-3-[(4-bromophenyl)methyl]-1-(3,5-dichlorophenyl)-2,3-dihydro-3-methyl-2-oxo-1H-imidazo[1,2-a]imidazol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:574934 HCAPLUS
DOCUMENT NUMBER: 137:140524
TITLE: Preparation of imidazo fused heterocycles as corticotropin releasing factor inhibitors
INVENTOR(S): Dubowchik, Gene M.; Han, Xiaojun; Vrudhula, Vivekananda M.; Zuev, Dmitry; Dasgupta, Bireshwar; Michne, Jodi A.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 321 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002058704	A1	20020801	WO 2002-US841	20020111
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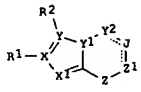
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2434558	AA	20020801	CA 2002-2434558	20020111
US 2002183375	A1	20021205	US 2002-44183	20020111
US 6888004	B2	20050503		
EP 1359916	A1	20031112	EP 2002-705754	20020111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EE 200300342	A	20031215	EE 2003-342	20020111
BR 2002006698	A	20040420	BR 2002-6698	20020111
CN 1499972	A	20040526	CN 2002-807135	20020111
JP 2004531475	T2	20041014	JP 2002-559038	20020111
ZA 2003005531	A	20040727	ZA 2003-5531	20030717
BG 107999	A	20040831	BG 2003-107999	20030717
NO 2003003350	A	20030922	NO 2003-3350	20030725
US 2004254382	A1	20041216	US 2004-767645	20040129
US 2004225130	A1	20041111	US 2004-771661	20040204
US 2004225001	A1	20041111	US 2004-771766	20040204
US 2004235924	A1	20041125	US 2004-772027	20040204
PRIORITY APPLN. INFO.:			US 2001-264570P	P 20010126
			US 2002-44183	A3 20020111
			WO 2002-US841	W 20020111

OTHER SOURCE(S): MARPAT 137:140524
GI

L4 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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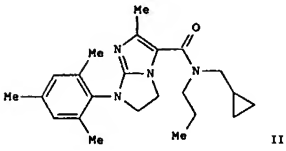
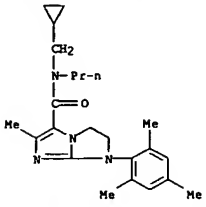


II

AB The title compds. [I; R1 = H, alkyl, haloalkyl, etc.; R2 = CONR3R4, CH2NR3R4, etc.; D = O, S; R3, R4 = H, alkyl, haloalkyl, etc.; or NR3R4 = 5-6 membered heterocycle; X = C; Y = C; X1 = N; Y1 = N; Y2 = N, CH, CH2, CO, etc.; J = a bond, CH, CH2, CO, etc.; Z1 = CH, CH2, CO, etc.; Z = NV (wherein V = (un)substituted Ph, 2- or 3-pyridyl)], useful for the treatment of depression, anxiety, affective disorders, feeding disorders, post-traumatic stress disorder, headache, drug addiction, inflammatory disorders, drug or alc. withdrawal symptoms and other conditions the treatment of which can be effected by the antagonism of the CRF-1 receptor, were prepared E.g., a 5-step synthesis of II (starting with 2,4,6-trimethylaniline) which showed Ki of < 1,000 nM against CRF1 receptor binding.
IT 444321-95-3P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of imidazo fused heterocycles as corticotropin releasing factor
inhibitors)
RN 444321-95-3 HCAPLUS
CN 1H-Imidazo[1,2-a]imidazole-5-carboxamide, N-(cyclopropylmethyl)-2,3-dihydro-6-methyl-N-propyl-1-(2,4,6-trimethylphenyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:123008 HCAPLUS
DOCUMENT NUMBER: 136:167376
TITLE: Novel preparation of (R)-3-(4-bromobenzyl)-1-(3,5-dichlorophenyl)-5-iodo-3-methyl-1H-imidazo[1,2-a]imidazol-2-one, an intermediate for antiinflammatory agents and immunomodulators
INVENTOR(S): Frutos, Rogelio P.; Johnson, Michael Dale
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012243	A2	20020214	WO 2001-US23996	20010731
WO 2002012243	A3	20020620		
W: CA, JP, MX				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2416906	AA	20020214	CA 2001-2416906	20010731
US 2002028949	A1	20020307	US 2001-918915	20010731
US 6414161	B2	20020702		
EP 1309595	A2	20030514	EP 2001-957358	20010731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2004505978	T2	20040226	JP 2002-518218	20010731
US 2002072615	A1	20020613	US 2002-76829	20020215
US 6433183	B2	20020813		
US 2002072610	A1	20020613	US 2002-77045	20020215
US 6441183	B2	20020827		
US 2002082441	A1	20020627	US 2002-77044	20020215
US 6458986	B2	20021001		
US 2002087009	A1	20020704	US 2002-77043	20020215
US 6437148	B2	20020820		

PRIORITY APPLN. INFO.:		US 2000-224166P	P 20000809
		US 2001-918915	A3 20010731
		WO 2001-US23996	W 20010731

OTHER SOURCE(S): CASREACT 136:167376; MARPAT 136:167376
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

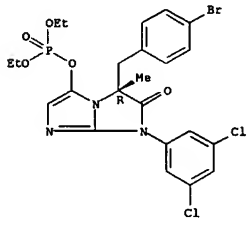
AB A novel process for the preparation of (R)-3-(4-bromobenzyl)-1-(3,5-dichlorophenyl)-5-iodo-3-methyl-1H-imidazo[1,2-a]imidazol-2-one I is disclosed. I is useful as an intermediate in the preparation of certain small mols. that are useful in the treatment or prevention of inflammatory and immune cell-mediated diseases. The invention also relates to certain intermediates used in the process. Cyclization of amino amide II with an isocyanatoacetate ester RO2CCH2NCO [R = C1-6 alkyl] using a

L4 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
triarylphosphine, a carbon tetrahalide, and a tertiary amine, gives III. Optional alk. hydrolysis of the resultant imidazolidinone ester III gives the acid III [R = H]. Cyclization of III [R = C1-6 alkyl] using a Lewis acid and a phosphine oxide, or cyclization of III [R = H] using a coupling agent, gives dione IV. Reaction of IV with a strong base and a chlorophosphate (R'O)2POCl gives an enol phosphate V, which is iodinated with Me3SiI or NaI/Me3SiCl to give I. In a specific example using R = R' = Et, a yield of 89% was obtained in the key cyclization of III (AlMe3 and Ph3PO), and 69% was obtained in the final iodination step (NaI/Me3SiCl).

IT **397329-89-4P**, Phosphoric acid (3R)-5-(4-bromobenzyl)-7-(3,5-dichlorophenyl)-5-methyl-6-oxo-6,7-dihydro-5H-imidazo[1,2-a]imidazol-3-yl diethyl ester
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1H-imidazo[1,2-a]imidazol-2-one derivative as intermediate for immunomodulators and antiinflammatory agents)

RN 397329-89-4 HCAPLUS
CN Phosphoric acid, (3R)-3-[(4-bromophenyl)methyl]-1-(3,5-dichlorophenyl)-2,3-dihydro-3-methyl-2-oxo-1H-imidazo[1,2-a]imidazol-5-yl diethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



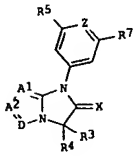
L4 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:78387 HCAPLUS
DOCUMENT NUMBER: 134:131538
TITLE: Preparation of imidazoimidazoles and triazoles as anti-inflammatory agents
INVENTOR(S): Wu, Jiang-Ping; Kelly, Terence Alfred; Lemieux, Rene M.; Goldberg, Daniel R.; Emeigh, Jonathan Emilian; Sorcek, Ronald J.
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 368 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001007440	A1	20010201	WO 2000-US18884	20000712
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6492408	B1	20021210	US 2000-604312	20000627
CA 2383017	AA	20010201	CA 2000-2383017	20000712
BR 2000012666	A	20020409	BR 2000-12666	20000712
EP 1216247	A1	20020626	EP 2000-948618	20000712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
TR 200200160	T2	20021021	TR 2002-200200160	20000712
JP 2003505460	T2	20030212	JP 2001-512524	20000712
EE 200200028	A	20030415	EE 2002-28	20000712
NZ 517217	A	20040227	NZ 2000-517217	20000712
AU 776496	B2	20040909	AU 2000-62091	20000712
BG 106312	A	20020930	BG 2002-106312	20020116
ZA 2002000428	A	20030117	ZA 2002-428	20020117
NO 2002000275	A	20020204	NO 2002-275	20020118
US 2003203955	A1	20031030	US 2002-195973	20020716
US 6689804	B2	20040210		
HK 1048637	A1	20050225	HK 2003-100839	20030206
US 2004116426	A1	20040617	US 2003-672412	20030925

PRIORITY APPLN. INFO.:		US 1999-144905P	P 19990721
		US 1999-150939P	P 19990826
		US 2000-604312	A1 20000627
		WO 2000-US18884	W 20000712
		US 2002-195973	A3 20020716

OTHER SOURCE(S): MARPAT 134:131538
GI

L4 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



I

AB Compds. I (A1 = N, CH; A2 = N, CH, CR'; R' = halo, cyano, alkoxy, alkoxycarbonyl, alkylsulfonyl; D = N, CH, CR1, C(SO2R1), C[S(:O)R1], C(CHO), C(SR1a), C(OR1a), C(NHR1a); R1, R1a = (substituted) alkyl, cycloalkyl, aryl, or heteroaryl groups, alkyl groups containing 2-6 carbons substituted with carboxylate, phosphonate, sulfonate, amidine, or guanidine moieties, amino, halogen, cyano; R3 = H, alkyl, cycloalkyl, alkoxy or amino substituted alkyl, cycloalkyl; R4 = substituted arylmethyl; R5 = Cl, F3C; R7 = H, halo, Me, cyano, O2N, F3C; X = O, S; if Z = N or CH, R7 = Cl, F3C, cyano, O2N; Z = N, CR6 where R6 = H, halo, Me, cyano, F3C), based mostly on imidazo[1,2-a]imidazole and imidazo[1,2-a]triazole nuclei, are prepared as inhibitors of the binding of leukointegrins to cell adhesion mols. in the treatment or prevention of inflammatory and immune cell-mediated diseases. E.g., (R)-I (A1 = N; A2 = D = CH; R3 = Me; R4 = 4-BrC6H4CH2; R5 = R7 = Cl; X = O; Z = CH) (II) was prepared from (R)-α-methyl-4-bromophenylalanine Me ester and 3,5-dichlorophenylisothiocyanate by heating in 1,4-dioxane to give a thiohydrantoin which was treated with N-(triphenylphosphoranylidene)-1,3-dioxolan-2-ylmethylamine [prepared from 2-(azidomethyl)-1,3-dioxolane and triphenylphosphine] to give a dioxolanylmethyliminoimidazolidinone derivative; treatment of the intermediate with trifluoroacetic acid and heating at 90° overnight gave II with m.p. 36-37.5°. I inhibited binding of leukointegrins to cell adhesion mols. with Kd<10 μM.

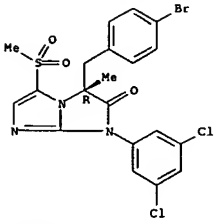
IT **321656-35-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of imidazoimidazole and imidazotriazole derivs. as inhibitors of leukointegrin binding to cell adhesion mols. in the treatment of inflammatory and immune-cell mediated diseases)

RN 321656-35-3 HCAPLUS

CN 1H-Imidazo[1,2-a]imidazol-2(3H)-one, 3-[(4-bromophenyl)methyl]-1-(3,5-dichlorophenyl)-3-methyl-5-(methylsulfonyl)-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

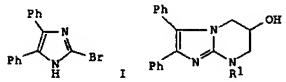
L4 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

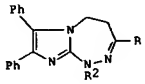
L4 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1982:406269 HCAPLUS
DOCUMENT NUMBER: 97:6269
TITLE: Synthesis of 5,6,7,8-tetrahydroimidazo[1,2-a]pyrimidine and 5,6-dihydroimidazo[1,2-a]-1,2,4-triazepine derivatives
AUTHOR(S): Priimenko, B. A.
CORPORATE SOURCE: Zaporozh. Med. Inst., Zaporozhe, USSR
SOURCE: Izvestiya Vysshikh Uchebnykh Zavedenii, Khimiya i Khimicheskaya Tekhnologiya (1982), 25(2), 149-51
CODEN: IVUKAR; ISSN: 0579-2991
DOCUMENT TYPE: Journal
LANGUAGE: Russian
OTHER SOURCE(S): CASREACT 97:6269
GI



I

II



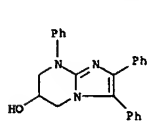
III

AB I was N-alkylated with epichlorohydrin or RCOCH2CH2Br, then cyclized with, resp., R1NH2 or R2NHNH2 to give, resp., II (R1 = Me2CHCH2, Ph, benzyl, m-tolyl) or III (R, R2 = Ph, Ph; p-tolyl, H; p-tolyl, p-tolyl).

IT **81974-72-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 81974-72-3 HCAPLUS

CN Imidazo[1,2-a]pyrimidin-6-ol, 5,6,7,8-tetrahydro-2,3,8-triphenyl- (9CI) (CA INDEX NAME)



L4 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN

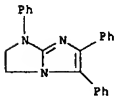
ACCESSION NUMBER: 1972:140642 HCAPLUS
DOCUMENT NUMBER: 76:140642
TITLE: Imidazoles. LXVI. Synthesis of 2,3-dihydroimidazo[1,2-α]imidazole derivatives
AUTHOR(S): Priimenko, B. A.; Kochergin, P. M.
CORPORATE SOURCE: Zaporozh. Gos. Med. Inst., Zaporozhe, USSR
SOURCE: Khimiya Geterotsiklicheskikh Soedinenii (1971), 7(9), 1252-4
CODEN: KGSSAQ; ISSN: 0132-6244
DOCUMENT TYPE: Journal
LANGUAGE: Russian
GI For diagram(s), see printed CA Issue.

AB ,3-Dihydroimidazo[1,2-a]imidazole derivs. were obtained by cyclization of 1-(β-hydroxyalkyl)-2-amino-4,5-diphenylimidazoles under the action of SOCl2 or POCl3, preferably in DMF. The same compds. were also obtained by reaction of 1-(β-haloethyl)-2-bromo-4,5-diphenylimidazoles with NH3 or primary amines. The following I were prepared (R, and % yield given): H, 43-61; Me, 71; C6H11, 53; PhCH2, 74; Ph, 40-74; m-MeC6H4, 54-57; p-MeC6H4, 56-68; p-HOC6H4, 68; p-MeOC6H4, 46-65; p-EtOC6H4, 46-79; m-ClC6H4, 65; p-ClC6H4, 76; p-BrC6H4, 72; and α-C10H7, 62.

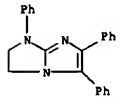
IT **25808-48-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 25808-48-4 HCAPLUS

CN 1H-Imidazo[1,2-a]imidazole, 2,3-dihydro-1,5,6-triphenyl- (8CI, 9CI) (CA INDEX NAME)



L4 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1970:90370 HCAPLUS
DOCUMENT NUMBER: 72:90370
TITLE: Synthesis of 2,3-dihydro derivatives of imidazo[1,2-a]imidazole systems
AUTHOR(S): Kochergin, P. M.; Povstyanoi, M. V.; Priimenko, B. A.; Ponomar, V. S.
CORPORATE SOURCE: Vses. Nauch.-Issled Khim.-Farm. Inst. im. Ordzhonikidze, Moscow, USSR
SOURCE: Khimiya Geterotsiklicheskikh Soedinenii (1970), (1), 129
CODEN: KGSSAQ; ISSN: 0132-6244
DOCUMENT TYPE: Journal
LANGUAGE: Russian
GI For diagram(s), see printed CA Issue.
AB Reaction of 2-haloimidazoles with halogenated alcs., olefin oxides, and 1,2-dihaloalkanes in an alkaline medium gave the following: 1-(2-hydroxyethyl)-2-bromo-4,5-diphenylimidazole m. 165-6°; 2-chloro analog, m. 138-9°; 2-chloro-3-(2-hydroxyethyl)naphth[1,2-d]imidazole m. 186-7°. These heated with NH3 or RNH2 gave: 1-(2-hydroxyethyl)-2-phenylamino-4,5-diphenylimidazole, m. 219-20°; 2-benzylamino-3-(2-hydroxyethyl)naphth[1,2-d]imidazole, m. 173-5°, which with SOCl2 gave: 1,5,6-triphenyl-2,3-dihydroimidazo[1,2-a]imidazole, m. 199-200°; 2,3-dihydroimidazo[1,2-a]benzimidazole (picrate, m. 180-2°); 1-benzyl-2,3-dihydroimidazo[3,2-b]naphth[1,2-d]imidazole. m. 186-7° (I). Similarly were prepared 1-(2-bromoethyl)-2-bromo-4,5-diphenylimidazole, m. 147-8°, and 2-chloro-3-(2-bromoethyl)naphth-[1,2-d]imidazole, m. 106-7°.
IT 25808-48-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 25808-48-4 HCAPLUS
CN 1H-Imidazo[1,2-a]imidazole, 2,3-dihydro-1,5,6-triphenyl- (8CI, 9CI) (CA INDEX NAME)



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L3          651 S L1 FULL

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L4           16 S L3

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